Remarks

Claims 1, 4-8, 14, 16-20, 49, 51-57, 60-64, 98 and 100-104 are currently pending in the application. Claims 2, 9, 10, 12, 13, 21, 22, 24-48, 59 and 65-93 have been withdrawn from consideration due to the Examiner's previous restriction requirement. Claims 3, 11, 15, 23, 50, 58, 94-97, 99, 105-106 have been canceled in a previous reply. These claims have been withdrawn or canceled without prejudice to, or disclaimer of, the subject matter thereof. Applicants reserve the right to file divisional and continuing applications directed to the subject matter of any claim withdrawn or cancelled for any reason.

By this response, Applicants do not acquiesce to the propriety of any of the Examiner's prior rejections and does not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 USPQ.2d 1865 (US 1997).

Applicants thank the Examiner for the reconsideration and removal of the rejection of the pending claims under 35 U.S.C § 112. The only remaining rejection is the rejection of the pending claims as obvious.

Claim Rejections under 35 U.S.C. § 103

The Examiner has sustained the rejection of Claims 1, 4-8, 14, 16-20, 49, 51-57, 60-64, 98 and 100-104 under 35 U.S.C. § 103 as obvious over United States Patent Number 5,547,979 ("Christensen") in view of the Merck Manual. OA at 3. According to the Examiner, Christensen teaches "the phosphodiesterase inhibitor[] rolipram . . . in a method of treating stroke in a human." *Id.* The Examiner also notes that: "The active ingredient may be administered from 1 to 6 times a day or as recognized by one of ordinary skill in the art that the optimal quantity and spacing of individual dosages will be determined by the nature and extent of the condition, the form, route, site of administration, patient, and that such optimums can be determined by conventional techniques." *Id.* The Examiner further states that: "the limitations regarding 'which enhances CREB pathway function' and 'wherein rehabilitation of said cognitive deficit is effect by producing a long lasting performance gain' are given little patentable weight because these biological processes are inherent when the same compound is administered in the same patient population at the same dosage." *Id.* at 3-4.

The Examiner concedes that Christensen fails to disclose "multiple cognitive training sessions sufficient to produce an improvement in performance of a cognitive

task whose deficit is associated with a central nervous system disorder." OA at 4. However, the Examiner posits that this failing of Christensen is remedied by the Merck Manual. According to the Examiner, the Merck Manual teaches that "a training protocol should be started as early as possible towards a patient's rehabilitation to stroke. Such rehabilitation includes encouragement, orientation toward the outside environment, eating, dressing, toilet functions, other basic needs, passive exercise, particularly of paralyzed limbs, and breathing exercises." *Id.* The Examiner concludes that these rehabilitation techniques meet the limitation of cognitive training and also notes that "it is obvious to one of ordinary skill in the art to not stop at a single training session in the rehabilitation of a stroke victim since the process takes a great deal of time with many repeated sessions." *Id.*

The Examiner continues that a person of ordinary skill in the art would have two reasons to combine the cited references: "(1) both Christensen and the Merck Manual disclose treatment for the same purpose, which is treating stroke patients and because (2) of the additive therapeutic effects of employing two methods of treating stroke simultaneously." OA at 5. The Examiner concludes that it would have been obvious "to have combined the cognitive multiple training sessions, as described in the Merck Manual, before and during administration of the phosphodiesterase inhibitor, rolipram, in the method of treating stroke in a human, as disclosed by Christensen." *Id.* Applicants respectfully traverse.

To maintain a proper rejection under 35 U.S.C. § 103, the Examiner must meet four conditions to establish a *prima facie* case of obviousness. First, the Examiner must show that the prior art suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, the Examiner must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Fourth, if an obviousness rejection is based on some combination of prior art references, the Examiner must show a suggestion, teaching, or motivation to combine the prior art references ("the TSM test"). *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Following *KSR Int'l Co. v. Teleflex, Inc.*, this fourth prong of the prima facie

obviousness analysis must not be applied in a rigid or formulaic way such that it becomes inconsistent with the more flexible approach of *Graham v. John Deere*, 383 U.S. 1, 17-18 (1966). 127 S. Ct. 1727 (2007). It must still be applied, however, as the TSM test captures the important insight that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* citing *United States v. Adams*, 383 U.S. 39, 50-52 (1966).

Applicants first note, that it has responded to these rejections on multiple occasions and incorporates by reference its prior responses to these rejections into this Reply. Specifically, Applicants maintain and incorporate their arguments presented in their response dated February 6, 2008.

The Examiner's response to those arguments misses the main thrust of Applicants' arguments. Importantly, Applicants claim "[a] method of increasing performance gain during treatment of a cognitive deficit." Applicants do not claim the phosphodiesterase inhibitor compounds themselves. Applicants also do not claim the general treatment of stroke patients via cognitive training. Rather, Applicants have invented and claim a particular method focused on stimulating particular biological pathway(s) to enhance cognitive function. Boiled down to its essence, it is Applicants' position that a reference (Christensen) that does not recite or in any way suggest or identify phosphodiesterase 4 or the CREB pathway[1] simply cannot disclose or fairly suggest the treatment of a cognitive disorder by inhibiting phosphodiesterase 4 in order to enhance CREB pathway, as Applicants currently claim.

The Office Action attempts to improperly bridge that gap in two ways. First, the Examiner argues that since Applicants' disclosure shows that rolipram is a phosphodiesterase inhibitor, that Christensen inherently discloses "administering a phosphodiesterase inhibitor." Second, the Examiner argues that the limitations regarding "which enhances CREB pathway function" and "wherein rehabilitation of said cognitive deficit is effect by producing a long lasting performance gain" are given

[1] As Applicants' argued in their prior response, it is simply undeniable that Christensen relates to the treating various "disease states mediated or exacerbated by TNF production." Christensen, Abstract. Indeed, Christensen's methods all focus on the administration of a "TNF inhibiting amount" of a compound. *See, e.g., id.* Col 2, ll. 10-20. Regarding stroke particularly, Christensen relates to the idea that TNF has pro-inflammatory activities, which "together with its *early* production (during the *initial* stage of an inflammatory event) make it a likely mediator of tissue injury in several important disorders including... stroke." *Id.* Col. 6, ll. 20-26 (emphasis added).

little patentable weight because these biological processes *are inherent* when the same compound is administered in the same patient population at the same dosage. OA at 3-4.

As Applicants argued in their prior response, inherency is not an appropriate basis for an obviousness rejection because "[t]hat which may be inherent is not necessarily known" and "[o]bviousness cannot be predicated on what is unknown." *Application of Shetty*, 566 F.2d 81 (C.C.P.A. 1977); *see also In re Rijckaert*, 9 F.3d 1531 (Fed. Cir. 1993). Moreover, the view that success would have been 'inherent' cannot substitute for a showing of reasonable expectation of success." *Application of Rinehart*, 531 F.2d 1048 (C.C.P.A. 1976). Stated differently, obviousness is based upon what the references disclose to one of skill in the art at the time of filing. The Examiner must demonstrate that rolipram was well-known in the art as a phosphodiesterase 4 inhibitor prior to Applicants filing date. The Examiner must also demonstrate that it was known in the art that rolipram "enhances CREB pathway function" and that rolipram in conjunction with the cognitive training "produc[es] a long-lasting performance gain." Quite clearly, the Applicants' own disclosure cannot be an appropriate source of that information. Thus, to the extent the Examiner relies on a theory of inherency to support the outstanding 35 U.S.C. § 103, such reliance is improper.

In short, neither Christensen nor the Merck Manual, either alone or in combination, provides any teaching or suggestion of a beneficial link between the inhibition of phosphodiesterases and cognitive training. Therefore, these references, singly or in combination, do not teach or suggest all of the claim limitations. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991).

For all these reasons and for all those reasons in Applicants' response dated February 6, 2008, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claims 1, 4-8, 14, 16-20, 49, 51-57, 60-64, 98 and 100-104 stand rejected under 35 U.S.C. § 103 as obvious over Christensen in view of the Merck Manual.

CONCLUSION

Applicants have properly and fully addressed each of the Examiner's grounds for rejection. Applicants submit that the present application is now in condition for allowance. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited. If there are any additional fees due in connection with the filing of this amendment, please charge the fees to undersigned's Deposit Account No. 50-1067. If any extensions or fees are not accounted for, such extension is requested and the associated fee should be charged to our deposit account

Respectfully submitted,

/djpelto Reg. No. 33754/

Date: **December 1, 2008**

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